STATUS OF CLAIMS

Claims 1-10, 15-18, 23-24, 29 and 31-32 are pending, of which, claims 1-2, 4-5, 9, 15, 17, 24, 29 and 31-32 are rejected. Claims 1 and 29 are the sole independent claims. Claims 11-14, 19-22, 25 -28 and 30 have been withdrawn as being drawn to non-elected inventions. Applicant has amended Claims 1, 24 and 29 and has canceled claims 31 and 32 herein. No new matter has been added by amending the claims.

REMARKS

Applicant thanks the Office for its reconsideration and withdrawal of previous 35 U.S.C. 112, second paragraph and 35 U.S.C. 102 rejections in light of Applicant's previous amendments to the claims and arguments.

However, the Office maintains its rejection of 35 U.S.C. 112, first paragraph and has therefore made this rejection Final. In order to further prosecution of this application on the merits, Applicant has amended the claims and respectfully request that this remaining rejection be withdrawn.

Rejection Under 35 U.S.C. 112, first paragraph

Claims 1-10, 15-18, 23-24 and 29 were rejected under 35 U.S.C. §112, first paragraph. The Office maintains that the specification "fails to describe in any fashion the physical and/or chemical properties of the claimed class of biosynthetic intermediates and/or metabolites thereof or class of ergostarol-biosynthetic enzymes..." The Office further argued that the claims do not enable the process of "producing prenyl compound by culturing any organisms having decreased desaturase activity and increase of any HMG-CoA reductase activity which overexpress any squalene expoxidase or sqalene epoxidase having 30% sequence identity to SEQ.ID.NO.:8 and any HMG-CoA reductase."

Applicant respectfully disagrees, however, in order to further prosecution of this application, Applicant has amended the claims such that the invention is directed to the production of ergosta-5, 7-dienol. Previously claimed intermediate and/or metabolites of ergosta-5, 7-dienol have been deleted from the claims. Throughout the specification, as

well as in the examples section of the application, Applicant has provided sufficient written description to enable one skilled in the art to produce ergosta-5,7-dienol.

The instant invention provides very detailed and elaborated information, not only about how to measure the respective enzymatic activity, but also how this activity can be modulated using standard genetic methods for increasing or decreasing a respective enzymatic activity in the genetically modified organism used in the invention. On pages 5-6 of the specification Applicant outlined the various ways in which to reduce the expression of the nucleic acid encoding Δ22-desaturase. Likewise, on pages 11-12 of the specification HMG-CoA-reductase, squalene expoxidase activities, to name a few, identifies several methods in which to accomplish the desired activity in order to produce ergosta-5,7-dienol.

It is further noted that the amended claim set (as well as the previously submitted claim set) is directed to *enzymatic activity* and not to any *percentage of identity.* Based upon these distinct differences it is irrelevant that the "predictability of which changes can be tolerated in protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification..." as argued by the Office. The enzymatic activity is well defined and any specific enzymatic structure showing a respective enzymatic activity in the tests, as described in the specification, are useful in the invention. Furthermore, it is well known in the art, that different microorganisms or cells show enzymatic activities for the same specific metabolic reaction, despite eventual structural difference in the enzymes themselves. Essential for the characterization of an enzyme are the functional properties, i.e., the enzymatic activity, and not the specific structure, because any specific structure having the claimed functional activity will effect the metabolic reaction necessary for producing ergosta-5,7-dienol. This is supported by the knowledge in the art as evident in a pre-published paper by Basson, Michael E., Molecular and Cellular Biology, volume 8, number 9, pages 3797-3808 (1988) (referred to herein as "Basson"), which states that "The pathway of sterol biosynthesis is highly conserved in all eukaryotic cells." In this paper a comparison is drawn between HMG-CoA reductase of a yeast strain and human cells. It is clear, that the enzymatic function is the same, although the enzyme of the different organisms differ in structural details.

For convenience, Applicant submit herewith references that support the argument that the enzymatic activity is independent of specific structure and specific organism.

1) Bochar, Daniel A. et al., Journal of Bacteriology, vol. 179, no. 11, pp. 3632-3638 (1997) – describes HMG-CoA reductase in a thermophilic archaeon.

2) Pena-Diaz, Javier et al., Biochem. J., vol. 324, pp. 619-626 (1997) - describes HMG-CoA reductase in a protozoan.

3) Bischoff, Kenneth M., Journal of Bacteriology, vol. 178, pp. 19-23 (1996) – describes HMG-CoA reductase activity in Escherichia coli.

4) Basson, Michael E., et al., Molecular and Cellular Biology, vol. 8, no. 9, pp. 3797-3808 (1988) – shows HMG-CoA reductase activity in human cells.

This same principle (i.e., the enzymatic activity is independent of specific structure and specific organism) is also applicable to other enzymes of the instant invention.

5) Tai, Hsin-Hsiung et al., Journal of Biol. Chem. vol. 247, pp. 3767-3773 (1992) – describes squalene epxidase of a rat liver.

6) Georgopapadakou, N.H., et al., Antimicrobial Agents and Chemotherapy, vol. 36, pp. 1779-1781 (1992) – describes squalene epoxidase activity in Candida albicans.

7) Nagumo, Akira et al., Journal of Lipid Research, vol. 36, pp. 1489-1497 (1995) - describes recombinant rat squalene epoxidase being expressed in E. coli.

8) Favre, Bertrand et al., Antimicrobial Agents and Chemotherapy, vol. 40, pp 443-447 (1996) – describes squalene expoxidase activity in dermatophyte fungi.

9) Robinson, Gordon W., Molecular and Cellular Biology, vol. 13, pp. 2706-2717 (1993) – describes squalene expoxidase in various organisms, inter alia human fibroblasts.

The list of references is just a few examples to support Basson's finding that "the pathway of sterol biosynthesis is highly conserved in all eukaryotic cells." Therefore, based upon these references and the amendments herein and in previous responses,

Applicant was clearly in possession of the invention at the time of filing as well as has enabled a person skilled in the art.

Furthermore, Applicant respectfully disagrees with the Office's argument that it is not routine in the art to screen for multiple substitutions or multiple modifications with reasonable expectation of success in obtaining this desired activity/utility. The present invention is not directed to a method for genetic modification in the organism, but rather to a method of producing a specific compound, ergosta-5,7-dienol using organisms which exhibit either a reduced or enhanced enzymatic activity, as claimed. Not only is it well known in the art how to increase or decrease enzymatic activity using standard genetic methods, such methods for achieving the claimed activity changes are described in detail in the specification as well as the dependent claims.

Therefore, based upon the amendments to the claims and the arguments put forth herein Applicant have satisfied all the requirements of 35 U.S.C. 112, first paragraph and respectfully request that this rejection be withdrawn.

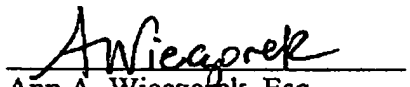
CONCLUSION

In light of the foregoing Amendments and remarks, it is believed that the rejections and objections of record have been obviated, and allowance of this application is respectfully solicited. If a telephone conference would facilitate examination of this application in any way, the examiner is invited to contact the applicant's attorney at (619) 846-4850. The Examiner's consideration of this matter is gratefully acknowledged.

FEES

The Commissioner is authorized to charge the fees for a petition for a three-month extension of time for a large entity ($1050), the RCE fee ($810) and any other fees deemed necessary in connection with the above-application to Deposit Account No. 50-1047.

Respectfully submitted,



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